

What is claimed is:

1. A method of modulating myostatin activation, comprising contacting a latent myostatin complex comprising a myostatin pro peptide and a myostatin C-terminal fragment, and a metalloprotease that can cleave the myostatin pro peptide, with an agent that increases or decreases proteolytic cleavage of the pro peptide by the metalloprotease, thereby modulating myostatin activation.
2. The method of claim 1, wherein the metalloprotease is a bone morphogenic protein-1/tolloid (BMP-1/TLD) family member.
3. The method of claim 2, wherein the BMP-1/TLD family member is BMP-1, TLD, tolloid-like protein-1 (TLL-1), or tolloid-like protein-2 (TLL-2).
4. The method of claim 2, wherein the BMP-1/TLD family member is BMP-1, mammalian TLD (mTLD), mammalian TLL-1 (mTLL-1), or mammalian TLL-2 (mTLL-2).
5. The method of claim 1, which comprises increasing myostatin activation, said method comprising contacting the latent myostatin complex and metalloprotease with an agent that increases proteolytic cleavage of the pro peptide by the metalloprotease, thereby increasing myostatin activation.
6. The method of claim 1, wherein said contacting is performed on a sample *in vitro*.
7. The method of claim 6, wherein the sample comprises a cell sample, a tissue sample, or a biological fluid sample.
8. The method of claim 1, wherein said contacting is performed *in vivo*, said method comprising administering the agent to a subject.

9. The method of claim 8, wherein the agent decreases proteolytic cleavage of the pro peptide by the metalloprotease, thereby reducing or inhibiting myostatin activation.

10. The method of claim 9, wherein, in the subject, muscle mass is increased, fat content is decreased, or a combination thereof.

11. The method of claim 10, wherein the subject is an animal raised as a food source.

12. The method of claim 11, wherein the animal is a mammalian species, an avian species, or a piscine species.

13. The method of claim 12, wherein mammalian species is an ovine species, a porcine species, or a bovine species.

14. The method of claim 12, wherein the avian species is a chicken or a turkey.

15. The method of claim 8, wherein the subject is a human subject.

16. A method of increasing muscle mass in a subject, comprising administering to the subject an agent that reduces or inhibits proteolytic cleavage of myostatin pro peptide by a protease, thereby preventing activation of latent myostatin and increasing muscle mass in the subject.

17. The method of claim 16, wherein metalloprotease is a bone morphogenic protein-1/tolloid (BMP-1/TLD) family member.

18. The method of claim 17, wherein the BMP-1/TLD family member is BMP-1, TLD, Tolloid-like (TLL) protein-1 (TLL-1), or TLL-2.

19. The method of claim 17, wherein the BMP-1/TLD family member is BMP-1, mammalian TLD (mTLD), mammalian TLL-1 (mTLL-1), or mammalian TLL-2 (mTLL-2).

20. The method of claim 16, wherein the subject is a vertebrate.

21. The method of claim 20, wherein the vertebrate is mammal.

22. The method of claim 21, wherein mammal is an ovine species, a porcine species, or a bovine species.

23. The method of claim 16, wherein the subject is a human subject.

24. The method of claim 20, wherein the vertebrate is an avian species.

25. The method of claim 24, wherein the avian species is a chicken or a turkey.

26. The method of claim 20, wherein the vertebrate is a piscine species.

27. A method for ameliorating a metabolic disorder in a subject, comprising administering to the subject an agent that reduces or inhibits the proteolytic cleavage of myostatin pro peptide by a protease, thereby preventing activation of latent myostatin and ameliorating the metabolic disorder.

28. The method of claim 27, wherein the metabolic disorder is a muscle wasting disorder.

29. The method of claim 28, wherein the muscle wasting disorder is associated with muscular dystrophy.

30. The method of claim 28, wherein the muscle wasting disorder is associated with cachexia.

31. The method of claim 30, wherein the cachexia is associated with cancer or acquired immunodeficiency disease.

32. The method of claim 28, wherein the muscle wasting disorder is sarcopenia.

33. The method of claim 27, wherein the metabolic disorder is obesity.

34. The method of claim 27, wherein the metabolic disorder is type II diabetes.

35. The method of claim 27, wherein the subject is a vertebrate subject.

36. The method of claim 35, wherein the vertebrate subject is a domesticated animal.

37. The method of claim 27, wherein the subject is a human subject.

38. A method of identifying an agent that modulates metalloprotease mediated activation of latent myostatin, comprising:

a) contacting a myostatin pro peptide, a metalloprotease that can cleave the myostatin pro peptide, and a test agent, under conditions sufficient for cleavage of the pro peptide by the metalloprotease; and

b) detecting a change in the amount of cleavage of the pro peptide in the absence of the test agent as compared to the presence of the test agent, thereby identifying the test agent as an agent that modulates metalloprotease mediated activation of the latent myostatin.

39. The method of claim 38, wherein the myostatin pro peptide comprises a latent myostatin complex comprising the myostatin pro peptide and a myostatin C-terminal fragment.

40. The method of claim 38, wherein the myostatin pro peptide comprises a latent myostatin complex comprising the myostatin pro peptide and a myostatin C-terminal dimer.

41. The method of claim 38, wherein detecting a difference in the amount of cleavage of the pro peptide comprises detecting the pro peptide or a cleavage product of the pro peptide.

42. The method of claim 41, wherein the amount of the pro peptide or cleavage product of the pro peptide is detected by electrophoresis, chromatography, or mass spectrometry.

43. The method of claim 41, comprising detecting an increased amount of a cleavage product of the pro peptide in the presence of the test agent as compared to an amount of cleavage product in the absence of the test agent, thereby identifying the test agent as an agent that increases metalloprotease mediated activation of the latent myostatin.

44. The method of claim 41, comprising detecting a decreased amount of the pro peptide in the presence of the test agent as compared to an amount of pro peptide in the absence of the test agent, thereby identifying the test agent as an agent that increases metalloprotease mediated activation of the latent myostatin.

45. The method of claim 41, comprising detecting an decreased amount of a cleavage product of the pro peptide in the presence of the test agent as compared to an amount of cleavage product in the absence of the test agent, thereby identifying the test agent as an agent that decreases metalloprotease mediated activation of the latent myostatin.

46. The method of claim 41, comprising detecting a greater amount of the pro peptide in the presence of the test agent as compared to an amount of pro peptide in the absence of the test agent, thereby identifying the test agent as an agent that decreases metalloprotease mediated activation of the latent myostatin.

47. The method of claim 38, further comprising determining an amount by which the agent modulates metalloprotease mediated activation of the latent myostatin.

48. The method of claim 38, wherein detecting a difference in the amount of cleavage of the pro peptide comprises detecting a change in myostatin mediated signal transduction in a cell expressing a myostatin receptor.

49. The method of claim 48, wherein the myostatin receptor is an activin receptor.

50. The method of claim 49, wherein the activin receptor is an activin type II receptor.

51. The method of claim 48, wherein the myostatin receptor is expressed from a transgene.

52. The method of claim 48, wherein the cell contains a reporter gene responsive to myostatin mediated signal transduction, and wherein said detecting comprises detecting a change in reporter gene expression.

53. The method of claim 52, wherein the reporter gene comprises a transforming growth factor-beta (TGF- β) regulatory element.

54. The method of claim 38, wherein the test agent is a peptide, a peptide hydroxamate, a phosphinic peptide, a peptoid, a polynucleotide, or a small organic molecule.

55. The method of claim 38, which is performed in a high throughput format.

56. The method of claim 55, which comprises contacting each of a plurality of samples comprising a myostatin pro peptide and a metalloprotease, with a test agent.

57. The method of claim 55, wherein the test agent comprises a plurality of test agents, and wherein at least one sample comprising a myostatin pro peptide and a metalloprotease of the plurality of samples is contacted with at least one test agent of the plurality of test agents.

58. The method of claim 57, wherein the plurality of test agents comprises a combinatorial library of test agents.

59. The method of claim 58, wherein the combinatorial library of test agents comprises a library of random test agents, biased test agents, or variegated test agents.

60. An agent identified by the method of claim 38.

61. An agent that modulates metalloprotease mediated activation of latent myostatin.

62. The agent of claim 61, which reduces or inhibits metalloprotease mediated activation of latent myostatin.

63. The agent of claim 61, which increases metalloprotease mediated activation of latent myostatin.

64. The agent of claim 61, which is a peptide agent, a polynucleotide agent, an antibody agent, or a small organic molecule agent.

65. The agent of claim 62, which is a peptide agent.

66. The agent of claim 65, wherein the peptide agent comprises a peptide portion of a myostatin polypeptide, or a derivative of said peptide portion.